

End-stage renal disease in India and Pakistan: Burden of disease and management issues

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End-stage renal disease in India and Pakistan: Burden of disease and management issues. In the absence of national registries, no reliable data are available on the incidence and prevalence of end-stage renal disease (ESRD) in India and Pakistan. The incidence of ESRD is likely to be higher than that reported from the developed world, with chronic glomerulonephritis being the most common cause, accounting for more than one third of patients, while diabetic nephropathy accounts for about one fourth of all patients in India. Patients are generally younger (mean age 42 years) at the time of detection of ESRD and two-thirds first see a nephrologist after they have reached end stage. Treatment of ESRD is a low priority for the cash-strapped public hospitals and in the absence of health insurance plans, less than 10% of all patients receive any kind of renal replacement therapy. The vast majority of patients starting hemodialysis die or stop treatment because of cost constraints within the first three months, and less than 2% patients are started on ambulatory peritoneal dialysis. Although renal transplantation is the cheapest option, only about 5% of all patients with ESRD end up having a transplant. Living related donor transplants constitute 30 to 40% of all transplants in India, but there is a conspicuous gender bias with female donors donating kidneys for their male relatives. Cadaveric transplantation has yet to pick up and accounts for less than 2% of all transplants. The enactment of legislation to regulate renal transplantation in India has not been able to prevent unrelated (paid) donor transplants, which constitute 60 to 70% of all renal transplants. Cyclosporine, azathioprine and prednisolone continue to be the backbone of post-transplant immunosuppression, with cyclosporine being stopped in a significant proportion at one year post-transplant to cut down costs. Increasing awareness of renal disease amongst the population and general practitioners could result in early diagnosis of chronic renal failure and give opportunity for preventive strategies to delay the onset of ESRD. Preemptive transplantation and use of generic cyclosporine can help bring down the costs of treatment. Innovative and affordable health insurance policies can also increase the number of patients who receive effective treatment for ESRD in these two countries.

Care of patients with end-stage renal disease (ESRD) in India and Pakistan, two countries that are home to more than one-sixth of the world's population, is largely guided by economic considerations. Having an annual

per capita gross national product (GNP) of \$450US and \$470US, respectively (less than 1.5% of that of the USA), both countries fall in the low income group and are classified as “developing countries.” With limited resources and less than 1% of their GNP spent on healthcare, the governments spend most of the allocated funds on more pressing issues such as population control, provision of clean drinking water and sanitation, and the control or eradication of communicable diseases. Therefore, it is understandable that ESRD care is a low priority for the cash strapped governments.

Both countries have a dual health care delivery system, with the economically less advantaged patients visiting the state run hospitals and the more affluent population generally patronizing hospitals in the private sector. State run hospitals—where consultations are generally free and dialysis and transplant costs subsidized—are overloaded with patients, with long waiting lists for starting dialysis as well as for undergoing transplantation. State run facilities do not provide maintenance hemodialysis for ESRD care, as most dialysis centers are overwhelmed by patients with potentially reversible acute renal failure. As opposed to this, privately run centers readily accept patients on maintenance dialysis programs and have a short waiting list for transplantation. Furthermore, all state run hospitals undertake kidney transplants only from genetically related or spousal kidney donors as opposed to the private sector where unrelated (and paid) donors are also accepted.

INCIDENCE AND CAUSES

In the absence of regional or national registries, the exact incidence of ESRD in both these countries is not known. The reported annual incidence from developing countries varies from 34 to 240 per million population (pmp) [1], which is in contrast to an incidence between 98 and 198 pmp per year reported from ESRD registries maintained in the developed countries [2]. There is no reason to believe that the incidence of ESRD will be lower in India and Pakistan than that reported from the

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Table 1. Causes of ESRD in India and Pakistan

	India ^a %	Pakistan %
Chronic glomerulonephritis	37	37
Diabetic nephropathy	24	10
Chronic interstitial nephritis	14 ^b	19
Hypertensive nephrosclerosis	13	12
ADPKD ^c	3.5	3
Multisystem	2.9	—
Miscellaneous	1.5	1
Unknown	3.8	18

Data from references 4 and 5.

^aMean age 42 ± 15.6 years

^bCalculus disease in 34%

^cAutosomal dominant polycystic kidney disease

West. In contrast, it is likely to be higher, with poor socioeconomic status predisposing the general population to a number of infection related glomerulonephritides (GNs) and a relatively higher incidence of nephrolithiasis, especially as both countries fall in the “stone belt.” A higher incidence of ESRD has been noted in Asians of Indian origin in Birmingham (UK), who comprise 14% of the population but 25% of dialysis patients and 30% of patients on the renal transplant waiting list; this is another pointer to the higher incidence of ESRD in this population [3]. Taking a conservative estimate of incidence of ESRD at 100/million population/year, and a population approaching 1.2 billion in these two countries, an estimated 120,000 fresh patients are likely to reach ESRD in both these countries every year. The prevalence figures are likely to be much lower, however, as most patients die due to lack of maintenance dialysis.

The causes of ESRD in India and Pakistan are shown in Table 1, with chronic GN the most common cause [4, 5]. The mean age of patients entering ESRD programs in the subcontinent is much lower (42 years) as compared to the West (61 years) [2]. Therefore, ESRD affects patients in the most productive years of their lives, and these patients are often the sole bread earners of their families. The lower mean age of patients with ESRD at least could be explained in part by the delay in diagnosis and failure to institute strategies delaying progression of chronic renal failure (CRF) to ESRD, and by the lower frequency of diabetic nephropathy due to type 2 diabetes mellitus.

Patients with CRF generally present late in the course of their disease, with 66% patients first seeing a nephrologist when they are already in ESRD. Although in the developed and industrialized world, access to renal replacement therapy (RRT) is unrestricted and easily available, patients in India and Pakistan often have to travel long distances to reach a kidney center because of maldistribution of renal services in India, with most of the centers located in large cities. Furthermore, because of the virtual absence of health insurance plans, less than 10% of all patients with ESRD receive any

kind of RRT. Most patients entering RRT programs in the country are funded by their employers or by charity organizations. In a study from a private sector hospital in south India, 63% patients belonged to this group, 30% arranged finances for their treatment by selling property, 20% raised loans and only 4% were able to take care of their treatment costs solely by pooling in family resources [6].

DIALYSIS

As compared to 72 dialysis centers in Pakistan (0.5 pmp) [7], there are an estimated 400 dialysis units in India (0.4 pmp) with about 1000 dialysis stations, more than two thirds being in the private sector. The annual cost of hemodialysis at private hospitals can vary between \$2500US/year for twice weekly hemodialysis to \$3500US/year for thrice weekly hemodialysis. This along with the cost of 6000 IU/week for erythropoietin (~\$2500US/year) ensures that the cost of maintenance hemodialysis is more than ten times the annual per capita GNP and, thus, is out of reach of the vast majority of the population. Of the patients who are started on dialysis, 69 to 71% die on dialysis or stop treatment (due to financial reasons), the majority within the first three months of initiation of dialysis, and only 17 to 23% patients end up having a kidney transplant. Of the 8 to 10% who continue to be on hemodialysis, 60% receive irregular treatments. Only 2 to 4% are started on continuous ambulatory peritoneal dialysis (CAPD) [8, 9]. These data are from centers known for their prolific transplant activity, and the overall percentage of ESRD patients undergoing a transplant is therefore likely to be only around 5%.

Most public sector hospitals and a majority of the private sector dialysis units provide hemodialysis for four hours twice a week using cellulosic membranes. All dialysis units reuse dialyzers after manual cleansing and more than 80% of dialysis units continue to use acetate buffer for hemodialysis. The dialysis prescription is generally empirical with Kt/V <1 in the majority [9].

Infections are common in patients on dialysis and are related to inadequate dialysis, malnutrition, and frequent use of blood transfusions to correct anemia. Together, uremic complications and infections account for 57% of all deaths in Indian patients on dialysis, with less than 30% of deaths due to ischemic heart disease [9]. The prevalence of hepatitis B and C virus infections varies between 4 to 12% and 4 to 16%, respectively, in Indian patients on dialysis and can lead to long-term sequelae in the post-transplant period.

The last five years have shown an impressive 50% annual growth in the number of CAPD patients in India, but this growth has not been so marked in Pakistan [7]. It is estimated that there are currently 1500 patients on CAPD in India, and until recently most patients were

using the Y-set. With the very recent establishment of a manufacturing unit indigenously and also weaning off of Y sets by the industry, most patients on CAPD are now on twin bags. More than two thirds of patients are on three two-liter exchanges/day and the peritonitis rates are acceptable. Financial constraints prevent wider acceptability of CAPD, with its annual cost being approximately \$4500US/year for three exchanges per day. Only a handful of patients can afford a cyclor and, therefore, cyclor-assisted peritoneal dialysis has yet to make its presence felt in the sub-continent.

RENAL TRANSPLANTATION

Renal transplantation is not only the best form of RRT in terms of quality of life after reaching ESRD, it is also the least expensive option if cyclosporine, azathioprine and prednisolone immunosuppression are used. Successful renal transplant, therefore, provides the best hope for most patients with ESRD in this region. There are approximately 45 major centers (0.05 pmp) performing transplants in India and 12 (0.08 pmp) in Pakistan [5, 7], doing an estimated 3000 and 400 transplants every year, respectively. The cost of renal transplant surgery at a public hospital is approximately \$1000US only, which will cover the surgical fees, medications, consumables and in-patient hospital charges, but the same surgery is likely to cost two to three times more at a private center. The annual cost of cyclosporine and azathioprine immunosuppression is approximately \$2500US, and in most instances cyclosporine is tapered and stopped at one year electively due to financial reasons. A significant number of patients stop cyclosporine abruptly because of economic constraints and run a higher risk of acute rejection and graft loss as compared to those with a slow taper. At one center in Pakistan a successful transplant program is being run largely based on donations from non-governmental charity organizations and individuals, where immunosuppressive drugs also are provided free of cost. This successful experiment needs to be copied at more places in the sub-continent [5].

Living related donors constitute 30 to 40% of all kidney donors in India. The type of kidney donors in a state funded, living-related kidney transplant program has provided interesting data on the exploitation of females as donors in the society. In this study, 37% of all donors were mothers and the kidney went mostly to the sons (76%); 29% donors were sisters and 88% of the beneficiaries of these kidneys were brothers. In all 66.4% of the donors belonged to the fairer sex, and 83.2% of all recipients were males [10]. Spouse donors (largely wives) account for more than 15% of all donors from within families.

Although India has the Human Organ Transplant Act in place since 1994 to regulate transplant activity and to

promote cadaveric transplants, there is no such legislation in Pakistan. However, despite the presence of this legislation, cadaveric donor transplantation has not picked up and accounts for less than 2% of all transplants that are being done. In Pakistan only a handful of cadaveric kidney transplants have been performed by transplanting organs donated from overseas organ-sharing networks [5]. The transplant community itself has not done enough to promote such activity. Lack of infrastructure such as motorable roads, communications and connectivity by air have impeded development of an organized organ-sharing network at a national level. Although most religions, including Islam, do not forbid cadaveric organ donation, lack of awareness about brain stem death, shortage of intensive care unit beds, social beliefs and illiteracy are the other obstacles to cadaver organ donation.

The Human Organ Transplant Act has not had the desired effect on the number of paid unrelated donor transplants, which constitute 60 to 70% of all transplants in India. 'Authorisation Committees' constituted under the Act, which are expected to allow transplantation of an organ from an unrelated donor only after they are 'satisfied' that the organ donation is solely for altruistic gains to the donor, have not been effective in controlling this activity.

PROMISE FOR THE FUTURE?

Problems of poverty and malnutrition cannot be easily solved by the politicians and economists of the region (much less by the nephrologists); however, an increased level of awareness of renal disease among the population and general practitioners can result in early diagnosis of CRF and preventive strategies implemented to delay the onset of ESRD. Indigenous manufacture of dialysis machines and disposables and effective reuse of dialyzers and tubings can help bring down the costs of hemodialysis. In both countries where majority of the population depends upon state-subsidized hospitals, chronic hemodialysis or CAPD are not likely to be viable large-scale RRT programs. Renal transplantation thus remains the best and least expensive option for RRT, and pre-emptive transplantation in patients with well-matched related donors can substantially reduce costs of treatment. Further, use of generic cyclosporine and planned co-administration of drugs that increase the bioavailability of cyclosporine, coupled with gradual withdrawal of cyclosporine 6 to 12 months after transplantation in patients with haplo-matched related donors also can reduce costs of post-transplant immunosuppression. Cadaveric kidney transplantation has to be encouraged to provide kidneys to patients without willing and blood group compatible kidney donors from within their families; however, the higher costs of post-transplant immunosuppressive drugs required for such patients will be a major limiting factor.

Innovative and affordable health insurances policies with wider acceptability for the general population can go a long way in increasing the number of patients who receive RRT. Being a low priority area for state funding, non-governmental charity organizations can have a larger role to play in establishing centers for providing RRT to patients with ESRD. Despite these measures, expanding the pool of ESRD patients receiving successful RRT and becoming socially and economically productive citizens of these countries is likely to remain extremely difficult.

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